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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,179	09/10/2001	Satoru Okamoto	213701US0PCT	9582

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	17

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,179	OKAMOTO ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3, 16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Specification

The abstract of the disclosure is objected to because of the use of the phraseology often used in patent claims e.g., "comprises". Correction is required. See MPEP § 608.01(b).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and/or idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method utilizing a phage random peptide library of structure as recited in e.g., page 29 and a substance that inhibits a nonstructural protein 3, HCV serine protease (NS3 protease) as the biomolecule with E.coli as the organism does not reasonably provide enablement for a method of screening any type of

substance that interacts with any biomolecule using any type of peptide library or organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claim is not commensurate in scope with the enabling disclosure. The scope of the claimed invention is drawn to an undefined number of variables. The specification at e.g., page 26 of the Examples discloses a method by which a defined inhibitor from a phage random library is screened to determine its inhibitory effect for the HCV portions. It is not apparent from the examples as to its applicability to the wide range of biomolecule or any type of library and organisms. The showing in the examples is limited to specific peptide library, enzyme protease and E. coli expressing phage display specific peptides. Other than the specifically exemplified components of the methods, the disclosure simply provides general statements. One skilled in the art would have not deemed the specific examples of containing defined variables to be predictive to unidentified components, as broadly claimed. In a highly unexplored and very unpredictable art as fusion phage, protease enzymes and peptide library, one cannot make a priori statement. See Osawa et al (The Journal of Biological Chemistry) at page

31052, the abstract. It would take undue amount of experimentation for one skilled in the art to practice the claimed invention. The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands,* (U.S.P.Q. 2d 1400 (CAFC 1988). These factors are as follows: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of the claims.

1). The specification fails to give adequate direction and guidance in how to readily go about determining which other peptides besides those recited therein can be made into a fusion library, the different organisms the peptide can be transfected, the different numbers of biomolecules.

2). The specification failed to provide working examples for any type of biomolecule or organism or library of peptides, the method of making the different libraries and an expression vehicle that can accept a peptide library of undefined sequence and length without deleteriously affecting vectors and/or hosts being used.

3). The breadth of the claims encompasses a large diversity of organisms, library and inhibiting substances. It is well

known in the art, that it is often difficult to know what the expression level of specific peptides or peptide fusions is; in many cases, even an average measure of expression level is difficult to obtain. The diversity of the inserts is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert.

4). The state of the prior art is such that while techniques or the expression of determinants on the surface exist only for the well studied vectors as phages, receptor and its ligand, however, even with phages, limitations are known to exist. For example, there are phage vectors that could cause protein domains that contain disulfide bonds in their folded forms not to fold.

5). The art is inherently unpredictable because even one surface peptide is identified in a candidate genetic package it is not possible to predict what effect the insertion of a foreign sequence into the protein will have on the protein or the genetic package *a priori*. Likewise, it is not possible to predict which variations of amino acids or combinations of amino

acids would result in the proper expression of the protein and therefore proper contact with the target molecule. It is generally known that the conformational freedom that promotes binding, e.g., by modifying the peptides into the protein sequences, might be restricted which may likely perturb the function and stability of the fusion in ways difficult to predict and measure.

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined variables would display an inhibitory peptide that inhibits a binding biomolecule without undue experimentation. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

[It is suggested that applicants recite the biomolecule as the HCV as recited in the EXAMPLES].

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps before and after step (a). The two method steps recite only for selecting. It is not clear as to the steps prior to selecting a recombinant organism and the step by which selection is made for step (a) and its correlation to step (b). The preamble recites for a screening step which is not recited in the body of the claim. Step (b) is unclear as to the step by which an inhibitor can be selected from. The alternative selection is confusing. It is not clear as to the whether the same or different steps are involved in said alternative selection.

B). Claim 4 is indefinite as to the recited "random peptide-presenting E. coli".

C). Claim 6 is indefinite in the use of the alternative language. See claim 1, above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the

> differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-6 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over by Martens et al (The Jrnl. of Biological Chemistry).

Martens et al discloses a method of selecting inhibitory substance of E-selectin comprising using recombinant peptide display library to screen for ligands that bind to E-selectin (biomolecule, as claimed). See specifically the Experimental Procedures at page 21129. The highest affinity peptide is selected then determined for its inhibitory effect against a ligand binding to E-selectin. See page 21132 up to page 21135. The specific method steps of Martens employing specific components in the method anticipates or renders obvious the broad claimed invention. [When the interpretation of the claim(s) is or may be given one interpretation, a rejection under 35 U.S.C. 102 is appro-priate and given another interpretation, a rejection under 35 U.S.C. 103(a) is appropriate. See MPEP § § 2111-2116.01.]

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated O'Neill et al (Proteins).

O'Neil discloses a method for screening a substance inhibitor comprising selecting from a library of random peptides display on the surface of filamentous phage. The library was screened using platelet glycoprotein which mediates the aggregation of platelet thorough binding of fibrinogen. E. coli was used as the organism to which the random peptides on the surface of the phage is transfected. See the Materials and Methods at page 510, which describes the details of the method. The selected peptide from the library where then tested and screened for inhibition of fibrinogen binding to platelets and inhibition of platelet aggregation. The specific method steps of O'Neill employing specific components in the method anticipates or renders obvious the broad claimed invention.

[When the interpretation of the claim(s) is or may be given one interpretation, a rejection under 35 U.S.C. 102 is appro-priate and given another interpretation, a rejection under 35 U.S.C. 103(a) is appropriate. See MPEP § § 2111-2116.01.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Klein et al (6,255,059).

Klein discloses at col. 2, line 55 up to col. 3, line 34, an assay method for screening and identifying compounds that specifically interact with and modulate the activity of a cellular receptor or ion channel (biomolecule as claimed). The assay enables rapid screening of large numbers of polypeptides in a library to identify those polypeptides which agonize or antagonize receptor bioactivity. The method comprises using a library of recombinant cells, each cell of which include (i) a target receptor protein whose signal transduction activity can be modulated by interaction with an extracellular signal, the transduction activity being able to generate a detectable signal, and (ii) an expressible recombinant gene encoding an exogenous test polypeptide from a polypeptide library. By the use of a variegated gene library, the mixture of cells collectively express a variegated population of test polypeptides. The polypeptide library includes at least 10 different polypeptides, though more preferably at least 10-107 different (variegated) polypeptides. The polypeptide library can be generated as a random peptide library. Klein

at col. 8, lines 55-64 discloses another embodiment of a method in which the peptide library can be screened for members which potentiate the response to a known activator of the receptor. In this respect, surrogate ligands identified by the present assay for orphan receptors can be used as the exogenous activator, and further peptide libraries screened for members which potentiate or inhibit the activating peptide. Alternatively, the surrogate ligand can be used to screen exogenous compound libraries (peptide and non-peptide) which, by modulating the activity of the identified surrogate, will presumably also similarly effect the native ligand's effect on the target receptor. The surrogate ligand can be applied to the cells. The specific method steps of Klein employing specific components in the method anticipates or renders obvious the broad claimed invention.

[When the interpretation of the claim(s) is or may be given one interpretation, a rejection under 35 U.S.C. 102 is appro-priate and given another interpretation, a rejection under 35 U.S.C. 103(a) is appropriate. See MPEP § § 2111-2116.01.

No claim is allowed.

REASSIGNMENT OF LOCATION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit ***1639***.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
May 19, 2003